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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/336,672	06/17/99	HERRATH M	SCRIP1100

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ART UNIT	**PAPER NUMBER**
1636	8

DATE MAILED: 06/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/336,672	Applicant(s) Von Herrath
	Examiner WILLIAM SANDALS	Group Art Unit 1636

☒ Responsive to communication(s) filed on *Apr 20, 2000*.

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-36* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-36* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Objections

1. Claim 1 is listed in Paper No. 7, filed April 20, 2000 as being amended. It is not amended.

Response to Arguments

2. Arguments in Paper No. 7 filed April 20, 2000 regarding the rejection of claims 1, 2, 5, 7-11, 13, 16-23 and 26-31 under 35 USC 102 over WO 97/46253 and WO 95/21926 have been fully considered but they are not persuasive. The response to the arguments is contained in the rejection repeated below.

3. Arguments in Paper No. 7 filed April 20, 2000 regarding the rejection of claims 1, 2, 5, 7-11, 13, 16-23 and 26-31 under 35 USC 102 over Ally et al., WO 95/06718 and WO 98/24908 are found persuasive and the rejections are dropped.

4. Arguments in Paper No. 7 filed April 20, 2000 regarding the rejection of claims 1-31 under 35 USC 112, first paragraph have been fully considered but they are not persuasive. The response to the arguments is contained in the rejection repeated below.

5. Arguments in Paper No. 7 filed April 20, 2000 regarding the rejection of claims 6, 8, 17, 20, 27, 29 and 30 under 35 USC 112, second paragraph have been fully considered but they are not persuasive. The response to the arguments is contained in the rejection repeated below.

Specification

6. The use of the trademarks ACCUCHECK III and TWEEN have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. The corrections in Paper No. 7 did not address all instances of the trademarks found in the specification.

Claim Rejections - 35 USC § 112

7. Claims 1-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of diabetes in a mouse model system, does not reasonably provide enablement for treatment of any autoimmune disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a composition and method for treating or preventing an autoimmune disorder by administering a nucleic acid construct encoding at least one epitope from a self-antigen to an animal. While applicants have shown a method of treatment of diabetes in a mouse model system, they have not demonstrated a method of treatment of **any** autoimmune

disorder. In order to do so, undue experimentation is required. Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors. Many of these factors have been summarized in *In re Wands*, 858 F.2d 731, USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors as they apply to the instant claimed invention are as follows:

a- The quantity of experimentation necessary to reduce the instant claimed invention to practice would involve a development of a method of treatment for each autoimmune disorder.

b- Guidance is provided which demonstrates a treatment of a mouse model system for diabetes, along with experimental data for the treatment of diabetes in a mouse model system. Only prophetic guidance is provided for other autoimmune disorders.

c- The nature of the invention is complex. Treatment or prevention of diabetes by gene therapy is still in a developmental stage, and as such is highly unpredictable.

d- The prior art has taught the gene therapeutic treatment of diabetes with replacement of cells which will produce insulin. Induction of immunologic anergy toward insulin producing cells has only been prophetically taught as described in Giannoukakis et al. at page 2107, column 2, where they state "[i]ntervention aimed at limiting islet damage will become plausible only when more satisfactory risk prediction protocols are developed. However, some safe preventive measures have already been explored in animal models and may eventually be applied to humans."

e- Giannoukakis et al. have taught the unpredictability of the claimed invention at page 2117 column 2 where they state "[a] better understanding of the genetics, the environmental triggers, and the immunopathology of type I diabetes, together with the factors affecting islet engraftment, as well as allogeneic and xenogeneic tolerance and protection from immune destruction, is necessary for these approaches to find clinical use."

f- Therefore, given the analysis above, it must be considered that the skilled artisan would have needed to have practiced considerable non-routine, trial and error experimentation to enable the full scope of the claims.

8. ***Response to Arguments***

Arguments presented in Paper No. 7 assert that the rejection is based on "safety issues". The rejection is based upon the teachings of lack of enablement in the prior art. The quoted sections from Giannoukakis et al. above state very clearly that the animal models have not been established as predictive, and that the understanding of the immunology of tolerance is still poorly understood. This being the case, the burden is high upon the instant inventors to provide all of the necessary teachings for enablement of the invention. Therefore, the instant claims and specification do not provide enablement for the full scope of the claims as written.

Paper No 7. also asserts that the specification provides support for the use of animal models. The cited paragraph is general and provides support for the concept that an antigenic epitope recognized by the immune system of a species may also be recognized by the immune

system of another species. Teachings on the reactivity of an epitope in more than one species, does not provide teachings on how to practice immune suppression of an autoimmune disease.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 6-8, 17-21, 27-29, 30 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 6, 17 and 27 recite the limitation "biological response modifier". "Biological response modifier" is not an art recognized term, and no definition is provided in the claims and specification to inform one of skill in the art exactly what is meant by this term. As a result the claim is vague and indefinite.

12. ***Response to Arguments***

Paper No. 7 presents argument that the term "biological response modifiers" is defined in the specification. A listing of many biological response modifiers is given in the specification. However, the specification does not limit its definition to those few examples, and the term is not defined by the examples.

13. Claim 9 recites the limitation "nucleic acid construct" in line 2. There is insufficient antecedent basis for this limitation in the claim.

14. Claim 9 recites the limitation "biological response modifier" in line 3. There is insufficient antecedent basis for this limitation in the claim.

15. Claim 20 recites the limitation "biological response modifier" in line 3. There is insufficient antecedent basis for this limitation in the claim.

16. Claim 29 recites the limitation "biological response modifier" in line 1. There is insufficient antecedent basis for this limitation in the claim.

17. Claim 30 recites the limitation "regulatory element". "Regulatory element" is not an art recognized term, and no definition is provided in the claims and specification to inform one of skill in the art exactly what is meant by this term. As a result the claim is vague and indefinite.

18. ***Response to Arguments***

Arguments set forth in Paper No. 7 assert that the term "regulatory element" is defined at the specification at page 13 line 21 to page 15, line 2. At page 14, lines 23-27, merely provides a listing of items which may be a "regulatory element", leaving the term undefined.

19. claim 36 recites the limitation "non-pathogenic...Th lymphocytes". There is no definition in the claims or specification to support this limitation, and the term "non-pathogenic...Th lymphocytes" is not an art recognized term. The term is therefore vague and indefinite.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

21. (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

22. A new reference has been submitted in an information disclosure statement filed on April 20, 2000. This reference has been argued in Paper No. 7 that it does anticipate the instant invention. The reference has been included in a rejection under 35 USC 102 below, along with a response to the arguments in Paper No. 7.

23. Claims 1, 2, 5, 9-11, 13, 14, 16, 20-24, 26, 30-36 rejected under 35 U.S.C. 102(a) as being anticipated by Liu et al.

Liu et al. taught (see especially the abstract, introduction, materials and methods, the figures, and page 202, column 2) a plasmid which encoded an autoantigen known to cause autoimmune diabetes. The expressed antigen was used to tolerize an animal model and prevent or decrease autoimmune diabetes in the animal model. The expressed antigen was used to vaccinate the animal to produce a positive immune response. The antigen was expressed under the control of a CMV promoter.

24. ***Response to Arguments***

Paper No. 7 asserts that Liu et al. did not teach a "self-antigen". GAD65 was the expressed antigen, which is a "self-antigen" which is well known to be part of the autoimmune diabetes disease.

Paper No. 7 asserts that Liu et al. did not **specifically** teach that the method was for the treatment or prevention of an autoimmune disorder. Liu et al. state at the abstract "can be used

for the treatment of insulin-dependent diabetes mellitus". This statement makes it abundantly clear that the method is useful for treating a well known autoimmune disease.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claims 1-9, 11-20, 22-30 and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by WO97/46253.

WO97/46253 taught (see especially the abstract, pages 13, 16, 17, 19-22, 35-37 and example 4) a nucleic acid which encoded a self-antigen in a plasmid construct under the control of a promoter which was administered to a mouse model system to protect the mice from onset of autoimmune disorders. The construct comprised a nucleic acid sequence which encoded cytokines.

26. ***Response to Arguments***

Paper No. 7 asserts that WO97/46253 does not teach a composition which comprised a nucleic acid sequence which encoded cytokines. At pages 22, lines 22-25 WO97/46253 recites "[a]ncillary nucleic acid sequences coding for peptides known to stimulate, modify, or modulate a host's immune response, can be coadministered with the above-described antigens. Thus, genes encoding one of more of the various cytokines..."

Paper No. 7 asserts that WO97/46253 fails to teach the generation of a "positive regulatory immune response". At page 18, lines 5-6 WO97/46253 taught "desensitization includes by is not limited to, a switch from a 'Th1' to a 'Th2' response".

27. Claims 1, 4, 11,12, 15, 16, 22, 25, 26, 30 and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/21926.

WO 95/21926 taught (see especially the abstract, and pages 6-13) the administration of a plasmid vector which contained a nucleic acid which encoded a self-antigen, which may be myelin basic protein, to treat autoimmune diseases such as multiple sclerosis and the subject may be human.

Response to Arguments

Paper No. 7 asserts that the tolerance taught by WO 95/21926 refers to antibody responses. At page 18, lines 19-20 WO 95/21926 taught "[t]he tolerogenic amount of fusion immunoglobulin can also vary depending on whether a T-cell or B-cell tolerance is desired". Clearly, T-cell tolerance of the type of the instant invention is taught by WO 95/21926. This addresses the further argument that WO 95/21926 did not contemplate a positive regulatory response, demonstrating that WO 95/21926 contemplated both a Th1 and Th2 type of tolerization of the subject animal.

Conclusion

28. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on April 20, 2000 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

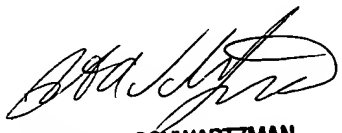
MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

29. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Friday from 8:30 AM to 5:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. George Elliott can be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

William Sandals, Ph.D.
Examiner
June 22, 2000



ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER